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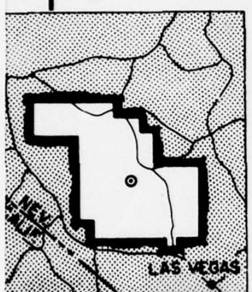

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Project 39.6a

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This is a preliminary report based on all data available at the close of this project's participation in Operation PLUMBBOB. The contents of this report are subject to change upon completion of evaluation for the final report. This preliminary report will be superseded by the publication of the final (WT) report. Conclusions and recommendations drawn herein, if any, are therefore tentative. The work is reported at this early time to provide early test results to those concerned with the effects of nuclear weapons and to provide for an interchange of information between projects for the preparation of final reports.

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Operation PLUMBBOB Preliminary Report

Project 39.6a

LARGE-ANIMAL NEUTRON-GAMMA IRRADIATION EXPERIMENT

By

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Approved by: R. L. Corsbie
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University of Tennessee-AEC Agricultural Research Laboratory

May 1958

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ABSTRACT

Eighty-eight burros were exposed to prompt neutron and gamma radiation from a nuclear detonation. Shielded from heat and missiles the animals were placed in 11 regularly spaced rows intended to bracket the median lethal dose of prompt radiation. The objectives of the experiment were to: (1) determine the median lethality response of the burro to the radiation described; (2) normalize the effect in the burro to that in the monkey; (3) compare weapon irradiation effects with those from isotopic gamma-ray sources; and (4) obtain preliminary measurements of the depth-dose pattern of radiation in a large mammal.

Postshot observations were made of clinical and pathological change. The median lethal dose was determined to be 402 rep ± 4 rep. Survival time and per cent were inversely related to dose level.

ACKNOWLEDGMENTS

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The problems associated with handling over one hundred adult burros through placement, recovery, and the postshot observation period are many and, for the most part, laborious. The Project Leaders particularly appreciate the voluntary and faithful labors of the following men:

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Chapter 1

INTRODUCTION

1.1 OBJECTIVES

The objective of this experiment was to expose a large animal (burro) to a nuclear detonation under conditions identical to the exposure of a smaller laboratory animal (monkey). The purpose was to compare the effects in the large animal with those in the small animal and, in turn, to make these data available for extrapolation to man for use in the estimation of the response of human beings to whole-body irradiation. There exists a large body of data on the response of burros to short- and long-term whole-body irradiation studies which may also be normalized in reference to the monkey and used in this extrapolation.

Specifically the objectives of the experiment were:

(1) Determination of the median lethality response of a large animal to neutron and gamma radiation from a nuclear detonation.

(2) Normalization of effects in the burro with those in another species, i.e., the monkey.

(3) Comparison of irradiation effects in the burro from a weapon detonation with those following short-term isotopic exposure.

(4) Preliminary measurement of the depth-dose pattern in a large mammal.

1.2 BACKGROUND

This experiment originated as a spontaneous outgrowth of a plan to expose burros to ionizing radiation similar to that expected in the crew compartment of a nuclear-powered aircraft. A unique opportunity existed in the program of the Civil Effects Test Group in Operation Plumbbob to

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expose large animals to a detonation that was being measured in the biological and physical terms of the Hiroshima explosion. It was possible to include the large-animal experiment at a late date because of the generous and helpful attitude of those directing and participating in the programs involved. The large animal project rode "piggyback" on the exposure planning of Project 39.6 and the dosimetry service of Projects 39.1 and 39.1b. In addition, the animal facilities of the Department of Defense, Military Effects Test Group, Project 4.1, and the laboratory facilities of Task Group 57 were made available for this study.

Chapter 2

MATERIALS AND METHODS

2.1 EXPERIMENTAL ANIMALS

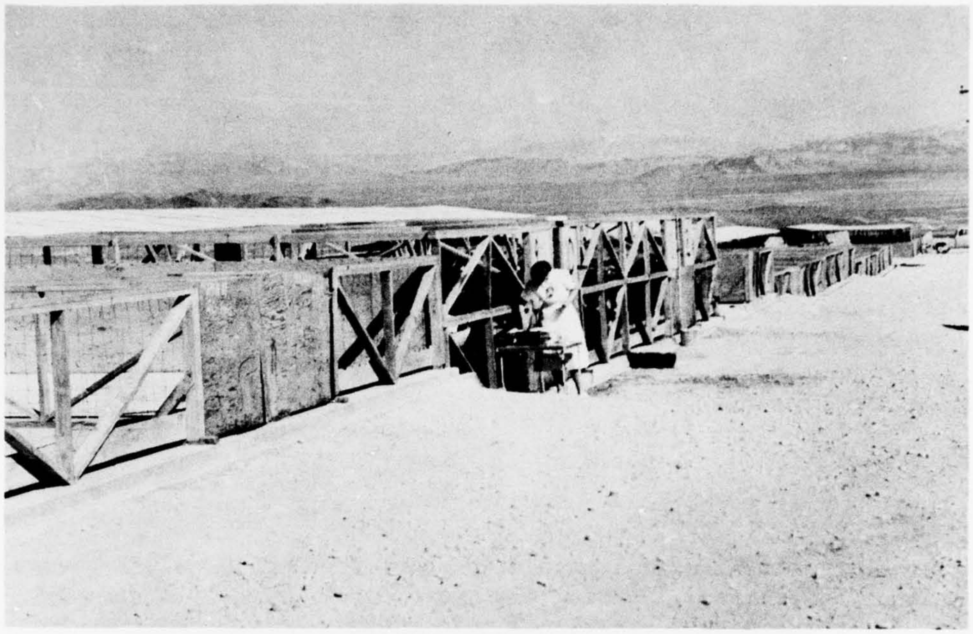
The experimental animal population consisted of 102 adult burros (60 male and 42 female). During the quarantine period, prior to exposure, the animals were base-lined with respect to age, weight, sex, hematology, ophthalmology, and general condition. Following this, animals were branded and lotted on the basis of sex, age, and weight into 11 groups of 8 animals each. Thirteen animals were maintained as on-site controls, and one animal was selected for a depth-dose study. All animals were kept in shaded or partly shaded concrete-floored pens (Fig. 2.1) and fed good quality alfalfa hay and oats throughout the study period. Animals were manually restrained consistent with good handling practices for bleeding and examination. One male burro was anesthetized, exsanguinated, and embalmed for purposes of the dosimetry study.

Following a postshot observation period of 2 months, survivor animals were removed by rail to the University of Tennessee-AEC Agricultural Research Laboratory, Oak Ridge, Tennessee, for continued observation.

2.2 EXPOSURE FACILITIES

Exposure facilities consisted of 44 sections of steel culvert pipe, each 5 ft in diameter and 13 ft in length, supported internally by 6 by 6 timbers. Shelters were designed to hold 2 animals placed nose to nose and broadside to the nuclear device.

The shelters were positioned in 11 rows of 4 each at regular slant-range distances calculated to bracket the radiation lethality range. One additional shelter was positioned in the front row to contain the dosimetry cadaver. Each shelter was anchored by means of six cables to two rows of deadmen approximately 12 and 16 ft in front of the shelter. In addition, each section was placed 6 in. below ground surface and toe-nailed to the earth by means of twelve 2.5-ft spikes.



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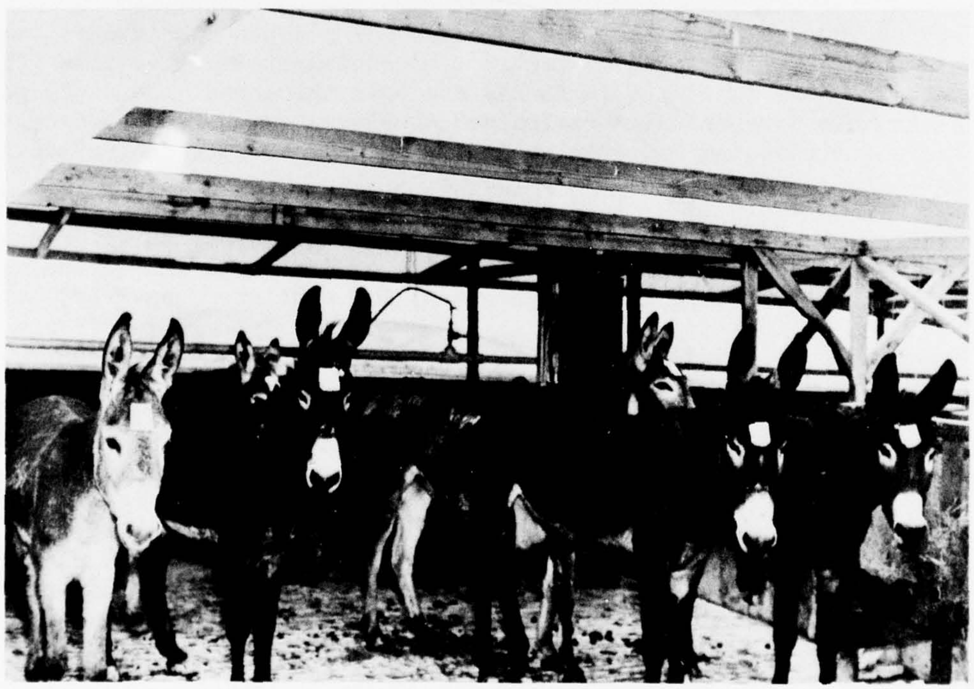

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Fig. 2.1—Animal holding pens. (a) Exterior view. (b) Interior view.

2.3 ANIMAL PLACEMENT AND RECOVERY

The animals were placed inside the exposure device immediately prior to the first scheduled H-hour and were satisfactorily maintained in position during a 48-hr period of schedule changes. Removal of the exposed animals was accomplished over a 5-hr period commencing approximately 4 hr postshot. The burro is by nature a stubborn animal; so ultimately the method of placement and recovery adopted utilized a sling arrangement lifted by a large self-propelled derrick (Figs. 2.2 and 2.3).

2.4 BIOLOGICAL MEASUREMENTS

Blood samples were collected from each animal at least twice prior to positioning. After the detonation the bleeding schedule was oriented by groups to intervals of 2 days for the first week and intervals of 3 and 4 days for the remainder of the on-site observation period. The examination of blood included hematocrit determination. White blood cell and differential counts were after methods described by Wintrobe.[1] Platelet counts were made by the Brecher-Cronkite method.[2] Clotting time and clot retractions were examined at selected intervals.

Necropsies were performed on all animals at death. Specimens taken for histologic study were fixed in 10 per cent neutral formalin and were stained with hematoxylin and eosin.

2.5 INSTRUMENTATION

2.5.1 Gamma Dosimetry

Gamma-ray dosimetry was furnished by Project 39.1. Measurements were made with chemical dosimeters in lithium shield assemblies. Dosimeter assemblies were placed in each of six rows positioned directly above the midline of the animals. In addition, film-pack dosimeters were placed at 10 separate locations in each of 25 animal shelters (see Fig. A.2).

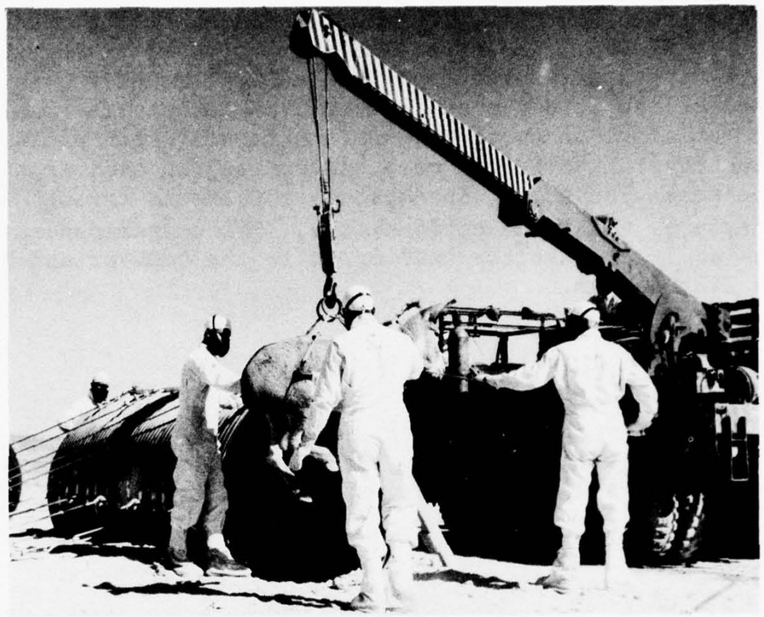
2.5.2 Neutron Dosimetry

Neutron dosimetry was furnished by Project 39.1b. This included fission-foil neutron-detector "goal-post" measurements and gold-foil assemblies (with and without cadmium covers) for depth-dose studies. A number of experimental germanium-crystal neutron dosimeters were obtained from Project 37.5 with the hope of obtaining fast-neutron depth-dose measurements and of augmenting the measurement of fast-neutron dose to live animals.

2.5.3 Depth-Dose Study

Three lithium-shielded chemical-dosimeter assemblies were implanted in the cadaver for depth-dose studies. The positions (Fig. 3.1) cor-

Fig. 2.2—Placing animals in exposure device.



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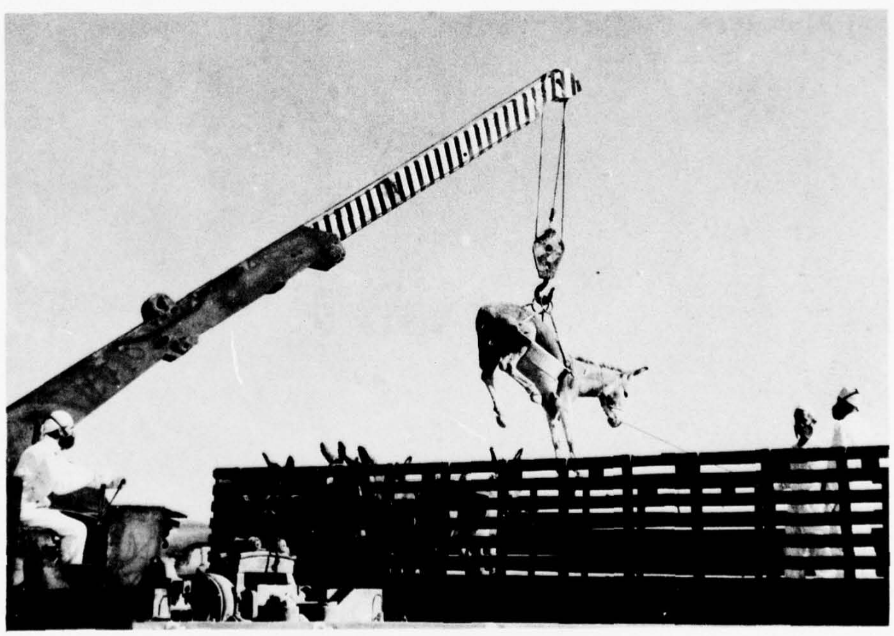


(b)

Fig. 2.3—Recovery operation, showing (a) detail of shelter and (b) loading technique.

respond to (1) a midline placement between the stomach and liver, (2) the medial surface of the 8th rib, and (3) medial to the space between the 15th and 16th ribs. The assemblies were secured rigidly by means of 10-gauge wire attachments extending vertically through the carcass. Gold-foil assemblies were placed adjacent to each of the chemical dosimeters and at eight other positions in a tissue-depth pattern. Fifty-six germanium crystal detectors were secured in the cadaver at the three chemical-dosimeter locations, in depth-dose patterns through the fore and hind quarters, and in selected organs. For comparison an air phantom was created in the shelter half opposite the cadaver and instrumented in a like manner.

2.6 PHOTOGRAPHY

A photographic record of the experimental study was made in 16-mm color moving pictures and in 4 by 5 black and white as an adjunct to the report of study methods and of changes seen in clinical symptomatology.

REFERENCES

1. W. M. Wintrobe, "Clinical Hematology," 2d ed., Lea & Febiger, Philadelphia, 1946.
2. G. Brecher and E. P. Cronkite, Morphology and Enumeration of Human Blood Platelets, J. Appl. Physiol., 3: 365-377 (December 1950).

Chapter 3

RESULTS

3.1 POSTSHOT FIELD OBSERVATIONS

3.1.1 General Observations

Exposure took place almost at the instant of detonation. The entire Project 39.6a experimental area was engulfed by the massive dust cloud. A reconnaissance was made at H + 1/2 hr. The area was bright with the morning sun and still. One animal was observed to be lying down, but it was easily roused; the remainder of the animals were standing quietly--much the same as during the evening prior to the detonation. The shelters had not been moved or otherwise affected by the blast and shock wave. Background radiation at the time varied between 50 and 200 mr from back to front of the area and was falling fast.

3.1.2 Recovery of Animals

Recovery of the animals began at the rear-most shelter at approximately 4 hr postshot. The animals were tractable and relatively easy to handle; however, within 1/2 hr one animal in the fourth highest dose line was observed to be in distress. An immediate inspection of the forward lines revealed a number of animals to be manifesting what appeared to be symptoms of delayed shock. One animal died at H + 5 hr. During the remainder of the 5-hr recovery operation on increasing number fell into shock. The affected animals were depressed. Those standing held the head low, ears and lips hanging; they were reluctant to move and were unsteady of balance. Those animals not standing could be roused, if at all, only with considerable effort and assistance. The last 20 animals were removed from the field prostrate or down.

At the holding pens the animals were unloaded, weighed, and quartered according to sex and dose group. Blood samples were obtained from four groups at 10 and 13 hr postshot.

3.2 DOSE MEASUREMENTS

3.2.1 Gamma-Neutron Dose

Six gamma-ray dose measurements made in burro shelters and three goal-post neutron measurements are available. Interpolated doses were obtained by the least-squares treatment of these data (Fig. A.1). The dose received by each group is tabulated according to type of radiation and total roentgen equivalent physical (1 rep = 93 ergs per gram of tissue) in Table 3.1.

Table 3.1—DOSE BY GROUP AND TYPE OF RADIATION

Exposure group	Gamma, rep	Neutron, rep	Total, rep
I	399	386	785
II	359	342	701
III	322	303	625
IV	288	268	556
V	260	236	496
VI	233	211	444
VII	210	186	396
VIII	188	165	353
IX	169	146	315
X	152	128	280
XI	136	114	250
XII	0	0	0

3.2.2 Film-badge Readings

Film-badge readings obtained from 10 stations in each of 24 shelters are in reasonable agreement with the expected decrease of radiation with distance and within the shelter. The station relationships with distance are given in Figs. A.2 and A.3.

3.2.3 Depth-Dose Data

Gamma-ray and thermal-neutron measurements obtained in the depth-dose study are shown in Fig. 3.1. The midline gamma-ray dose in the cadaver appears to be approximately 70 per cent of the air dose. Thermal-neutron measurements made in the cranial cavity and mouth are greater than those in the body by a factor of 2. Measurements of germanium-crystal neutron detectors used in this experiment have not been made available.

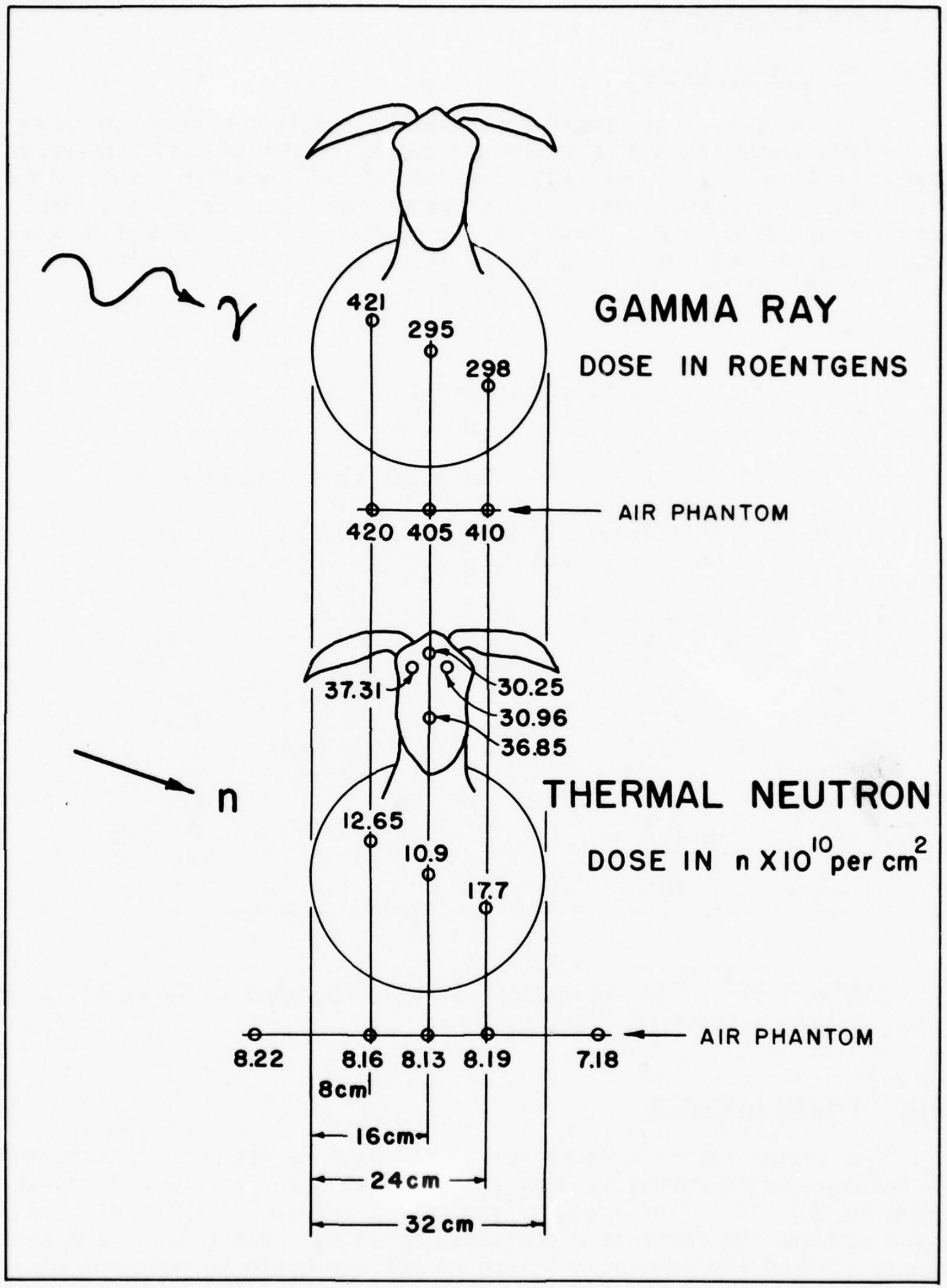


Fig. 3.1—Depth-dose response in rep and thermal neutrons/cm^2 in cadaver and air phantom.

3.3 MORTALITY RESPONSE

3.3.1 Pattern of Deaths

The response of the burro to the prompt radiation from the detonation was characterized by early mortality, 60 per cent of the deaths occurring within 48 hr postshot. By the end of the first week, over 80 per cent of the acute deaths had occurred; the remaining 16 per cent nonsurvivors died over a period of the next 35 days. One animal in group VI died at 58 days and another in group VII at 120 days. Survival data for all groups are given in Table 3.2.

Table 3.2—SURVIVAL BY GROUP

Group	Number surviving	Survival time of decedents: Mean, hr	Median, hr	Range, hr
I	0/8	21.7	20.5	18-32
II	0/8	23.1	20.0	16-41
III	0/8	34.1	27.5	5-72
IV	1/8		51.5	20-
V	1/8		176.0	24-
VI	1/8		25 days	17-
VII	2/8		13 days	48-
VIII	6/8			16-
IX	6/8			12 days
X	7/8			100
XI	8/8			

The severity of the mortality response appeared to be directly related to dose as shown in Fig. 3.2.

3.3.2 Median Lethality

The median lethal dose as determined from an arc sine transformation of the cumulative mortality data for 30 to 45 days was 402 ± 4 rep as shown in Fig. 3.3. Inclusion of one animal (group VI) dying at 58 days would perturb the cumulative mortality curve only slightly. From interpolated values the theoretical dose of 402 rep would be composed of 213 rep of gamma ray and 189 rep of fast neutron.

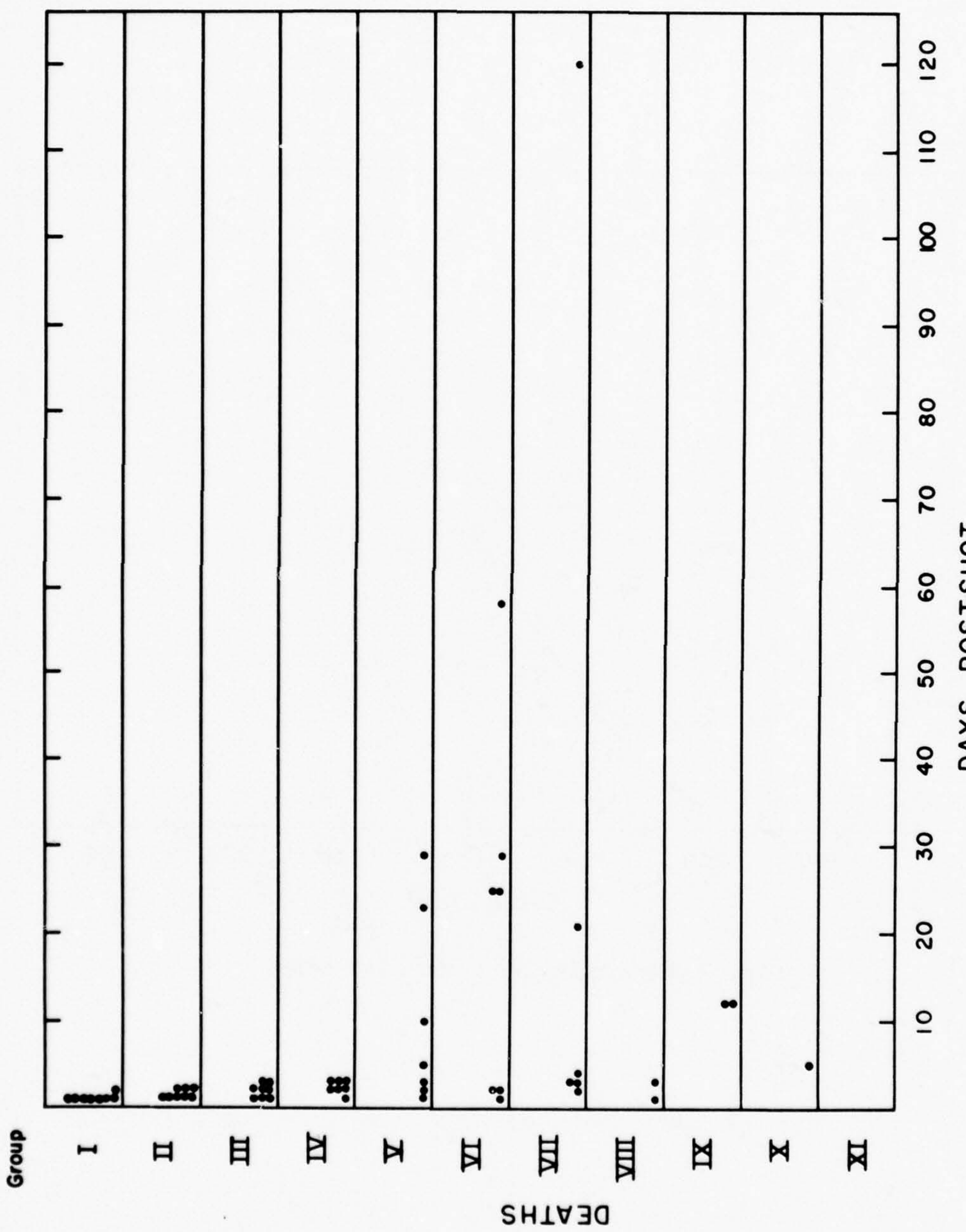


Fig. 3.2—Distribution of deaths by dose group.

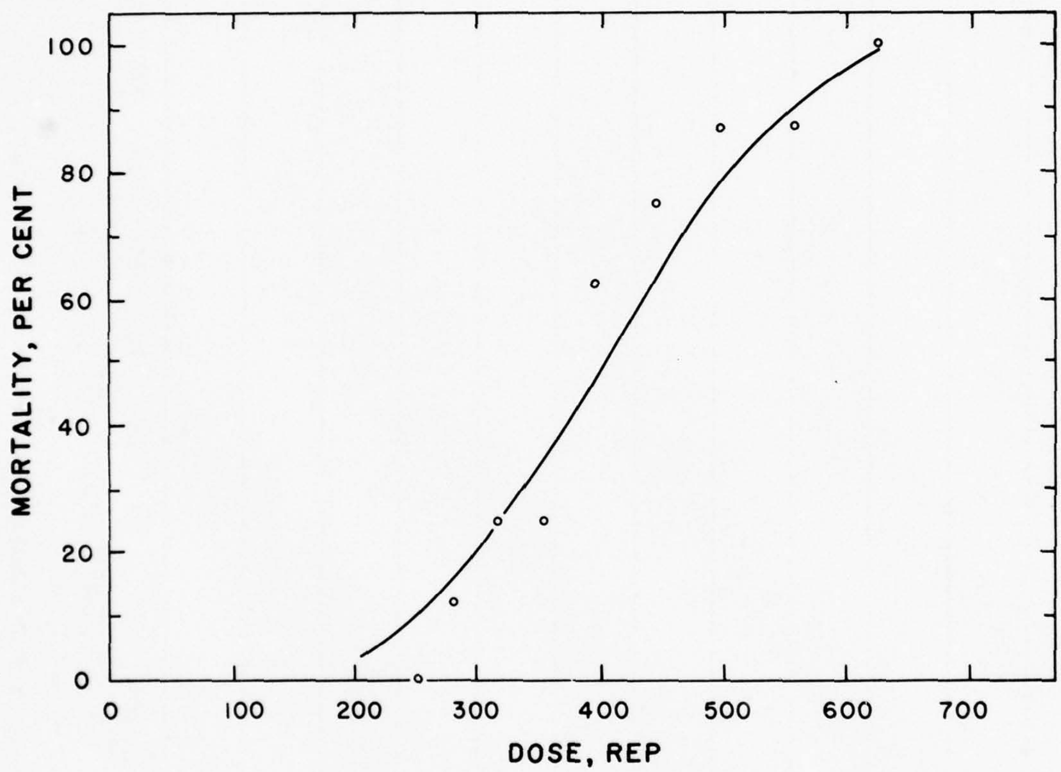


Fig. 3.3—Cumulative mortality data.

3.4 CLINICAL OBSERVATIONS

3.4.1 Early Behavioral Response

Early behavioral responses in the burro during the period of removal from the exposure field are noted in Sec. 3.1.2.

All animals, except those in the lowest dose group, stood or lay about numbly when returned to the holding pens. Eyes were swollen and lacrimating. Even though depression was profound in all, it was exhibited in greater degree by those animals in the higher dose groups. (Figs. 3.4 and 3.5.)

3.4.2 General Response

A majority of animals exhibited other neurological symptoms after the initial depression. During the first evening over one-half the burros in the highest dose groups had reached an agonal state; by morning 16 were dead (Figs. 3.6 and 3.7). Additional animals showed an increase in severe neurological symptoms which appeared to be dose related. Deaths continued during the 2d and 3d days; the sequence was as follows:

0 to 5 hr—1	49 to 72 hr—9
6 to 24 hr—18	73 to 96 hr—1
25 to 48 hr—14	97 to 120 hr—2

The last two animals to succumb prior to 120 hr were both quietly prostrate for a period of almost 3 days prior to death. Encephalitic symptoms were associated with terminal illness in separate cases as late as the 25th day. Anorexia was complete until the 2d day in the lowest dose group and until as late as the 6th day in surviving high-dose animals. Diarrhea, though not a notable sign, was observed in survivors at the end of the first week and generally lasted 1 or 2 days.

Wounds healed normally until shortly after the end of the first week. Suppuration of wounds was notable at this time but ceased to occur after the 9th postshot day. Between the 8th and 17th day prolonged bleeding from venipuncture and incidental wounds was indicative of a defect in clotting mechanism. Capillary fragility was increased through D + 35 days as evidenced by the occurence of petechial hemorrhage in mucous membranes following normal handling pressures.

Epilation became a notable sign as early as D + 12 and was generally observed in the majority of survivors by the end of the second week. The beginning of an epidemic of warts was detected in survivors of all but the lowest dose groups on D + 8. Symptoms suggestive of foot pain were observed variously from the 8th through the 32nd day. Nonspecific

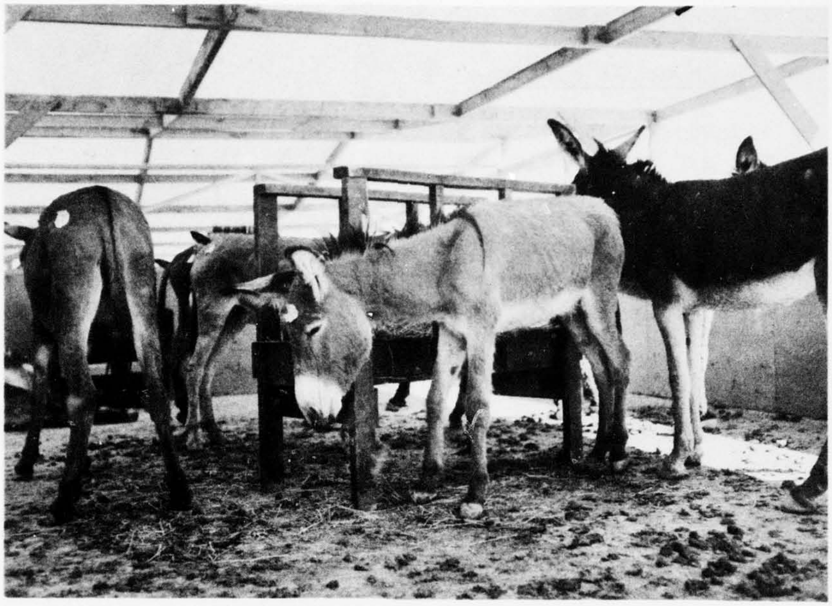


Fig. 3.4—Postshot depression in the high-dose groups. Note lacrimation of animal in foreground.

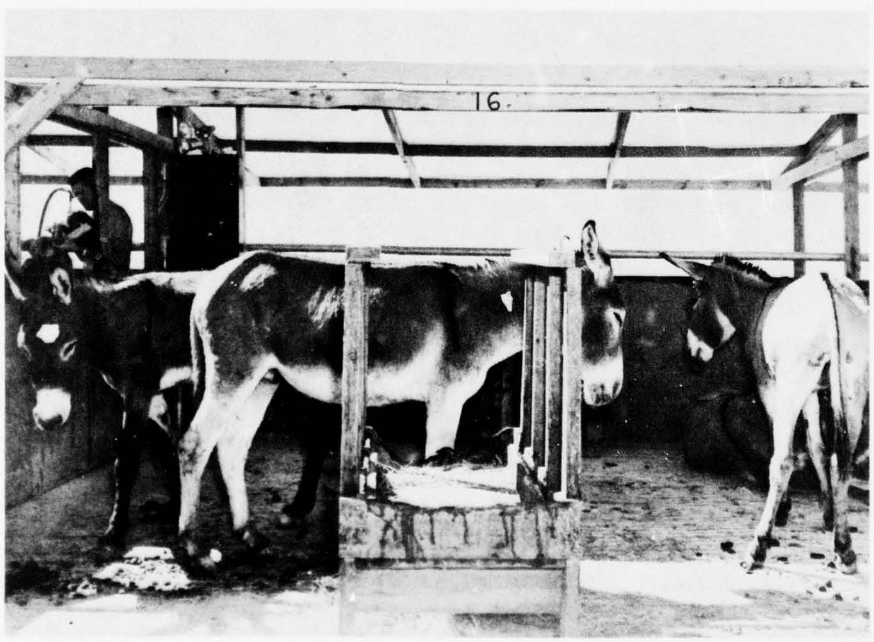


Fig. 3.5—Post detonation depression in the low-dose groups.

Fig. 3.6—Males, groups I and II, D + 1.

Fig. 3.7—Jennets groups I and II, D + 1. Note overturned water trough and position of decedent in background.

joint swellings were observed in several survivors at 8, 14, and 27 days postshot. Some apical gingivitis was observed as late as D + 40; however, ulcerations of the mucous membranes were not generally observed. Subjective evidence of recovery appeared inversely related to dose and began with a return of appetite. Throughout the course of the experiment the field control animals remained in excellent health. One animal exhibited a nonspecific swelling of the prepuce and scrotum which lasted 3 days but caused no apparent discomfort.

3.4.3 Neurological Symptoms

Neurological symptoms were striking and existed in several degrees. Deranged consciousness was manifested by irritability and hyperesthesia and by depression. Motor irritation was manifested by clonic muscular contractions, such as in those of the neck causing the head to bob rhythmically, by fibrillation of muscle groups, paralysis, nondirectional walking, and forward pressing. During the first 3 days affected animals staggered and leaned against solid objects for support. Affected animals commonly maintained a spraddle-legged stance during the first week to compensate for both muscular weakness and vertigo (Figs. 3.8 and 3.9).

An early sign following the initial period of lassitude was an irritableness seen on the 2d day in the lowest dose group and subsequently in all survivors. This was manifested by kicking and biting at the slightest or at no provocation and by extreme reaction to only slight pressure or other stimuli.

3.4.4 Neurological Symptoms by Group

In general, the animals in the first four dose groups exhibited neurological symptoms throughout the period of postshot survival.

One animal in group IV (556 rep) exhibited muscle tremor and mouthing on D + 3. After being down, in what appeared to be an agonal struggle, this animal regained her feet on D + 4 and made an eventual complete recovery.

Three animals in group V (496 rep) became hypersensitive and irritable in less than 24 hr postshot, kicking at slight provocation. Animals in this group, in general, showed muscle twitching and tremor within 2 or 3 days postshot. The subjective recovery of 1 of 4 animals in this group which survived past the first week was interrupted at the 9th day by pneumonia. During the rapid course of his terminal illness, he snapped and ground his molar teeth, exhibited symptoms of brain pressure, and collapsed and died abruptly.

Moderate depression was seen in 3 animals of group VI (444 rep). These succumbed within 28 hr. The other 5 animals appeared brighter

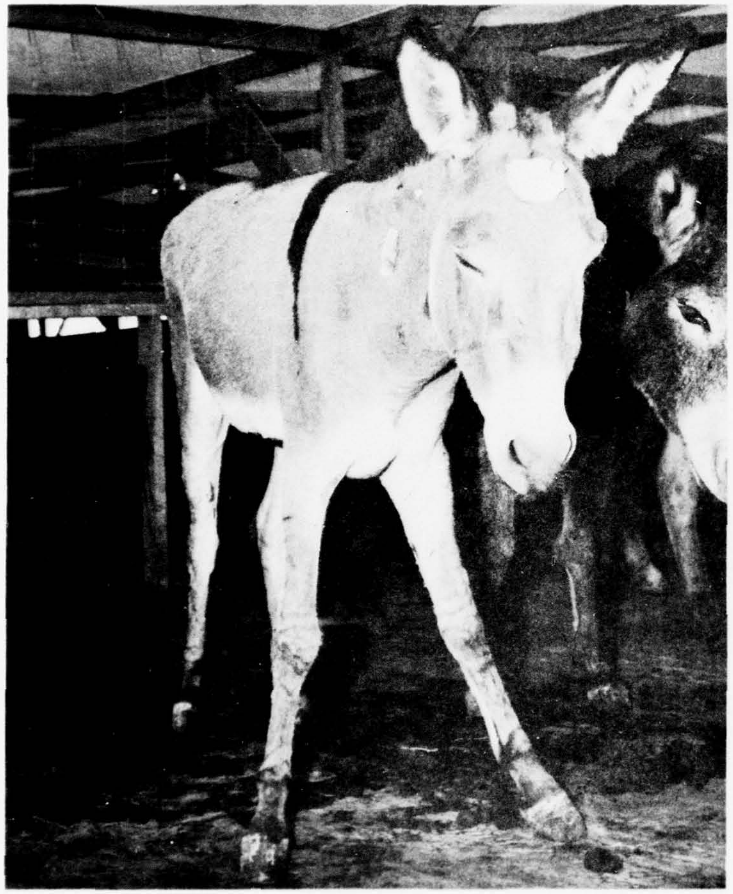


Fig. 3.8—Jennet No. 64, group IV, D + 2. Note spraddle-legged stance, swollen eyes, and lacrimation.

Fig. 3.9—Jack No. 9, group V, and No. 28, group VI, D + 3. Note pendulous lips, lacrimation, and drooling.

after the first day but exhibited muscle tremor, twitching, and incoordination within the next 3 days. One animal of this group showed signs of encephalitis prior to death on the 25th day. Moderate depression was also evident in group VII (396 rep) on D + 1--in general, some 14 hr later than seen in the highest dose groups. At this time all animals were notably irritable and twitching. One animal exhibited marked encephalitic symptoms, i.e., forward pressing, twitching, head-shaking, mouthing, and excitement. This animal died on D + 3. Two others died more quietly on the 3d and 4th days. No. 14 of this group manifested severe encephalitic symptoms on the 2d and 3d days, steadily pressing against the wire fencing of the holding pen to the point where the commissures of the lips were deeply cut. After an otherwise stormy course, this animal made a complete subjective recovery (Fig. 3.10).

In group VIII (353 rep) one animal exhibited signs of encephalitis and died 16 hr postshot. The other animals of the group became irritable and showed muscle twitching and tremor during D + 1. A second animal became moribund on D + 2; the remaining animals survived.

Depression in the lowest dose groups (315, 280, and 250 rep) was less profound. Animals in all three groups were irritable and showed muscle tremor and twitching on the 2d day postshot. Of the two most severely affected animals in group IX, one showed spasmodic orthochorea on D + 3. The other animal exhibited signs of brain pressure and in pushing against the fence wire caused severe lacerations of the face. This animal recovered from its nervous symptoms and died some 6 days later from causes associated with septicemia. One animal in group X went down on D + 2 and remained quietly prostrate until death, 2 days later. In group IX one of two animals dying on D + 12 exhibited encephalitic symptoms for one day prior to death. On the 25th day following the shot, one animal of group VI was observed with encephalitic signs prior to death.

3.4.5 Infections

Based on clinical observations alone several items are of interest concerning the occurrence and course of obvious infective processes in the experimental animals.

During the second week postshot one animal in group IX and another in group X were observed to have actively growing warts on their muzzles and lips. These papillomas were entirely similar to verruca vulgaris infections seen in equidae and consisted of elevated rough-surfaced nodules. During the next two weeks 20 animals in the remaining eight groups exhibited warts that were numerous in the extreme and confluent. The affected areas were swollen and fissured, weeping, and variously scabby (see Figs. 3.11 and 3.12). By the end of the observation period, the majority of cases showed a spontaneous regression of the papillomas. The animals of groups XI and XII (controls) at no time exhibited noticeable infection. Most of these animals had, prior to and during the periods

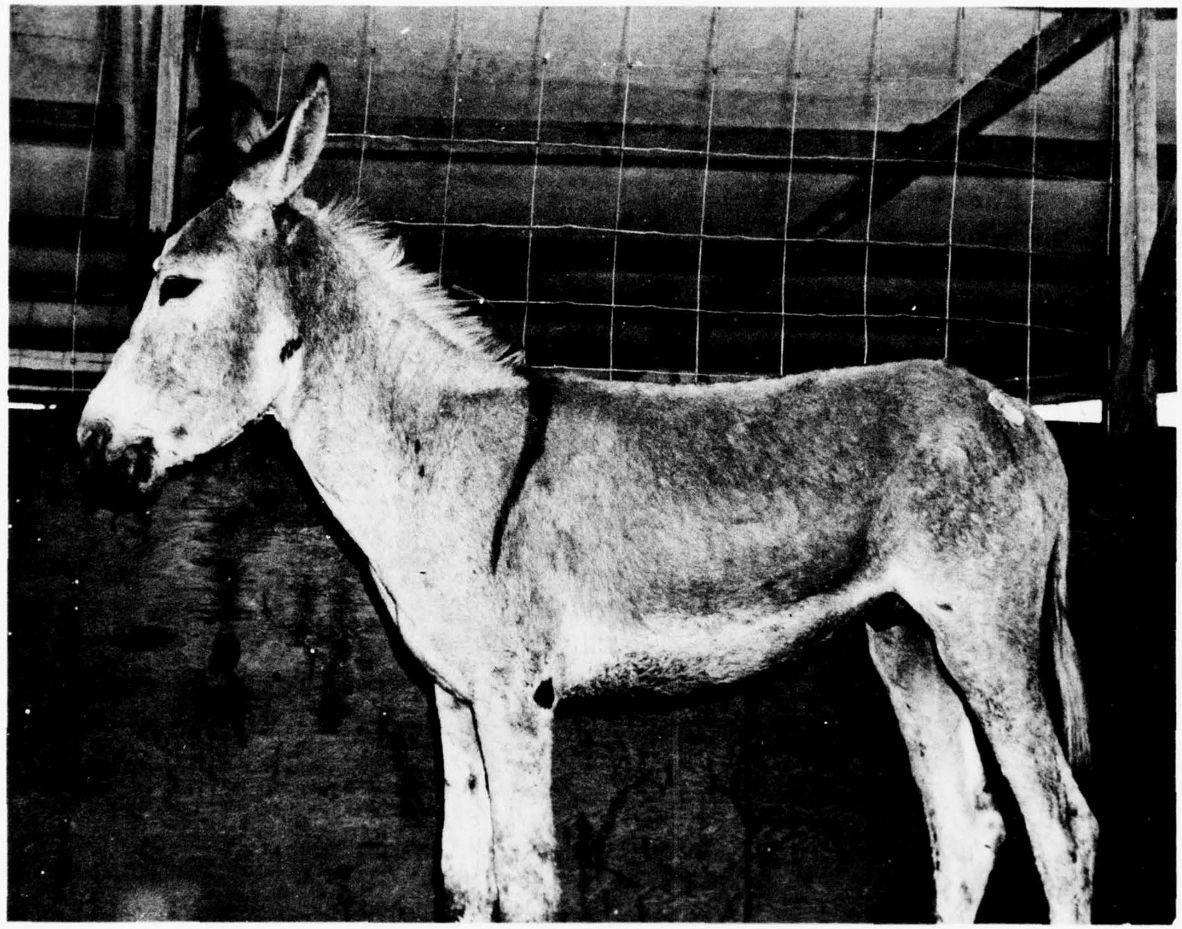


Fig. 3.10—Jack No. 14, group VII, D + 2. Note stilled attitude and paralyzed tongue. Animal is leaning against partition.

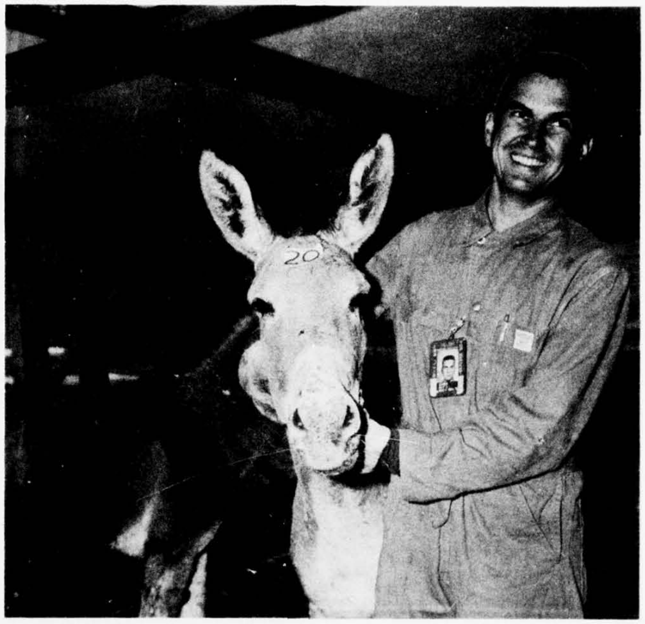


Fig. 3.11—Wart infection in group IX jack.

Fig. 3.12—Wart infection in group VI jack. Note extensive involvement of muzzle and orbital areas.

mentioned, smooth, pigmented, circumscribed areas either flat or only slightly raised suggestive of old healed wart areas.

Until the second week postshot normal wound healing and pus formation were seen. Superficial abrasions manifested a healing process under the eschar, and wounds that had been received when the animals were down had healed by the 9th to 10th day. On the 8th day postshot pus formation was observed to be remarkable in 4 animals and to a lesser degree in 3 others. A massive abscess developed on the face of animal No. 72 of group VII, previously mentioned as having sustained self-inflicted wounds, extending from the right eye to the lips involving two-thirds of the facial area (Fig. 3.13). Abscesses ruptured spontaneously in the mandibular space of burro No. 79, group VII, and from the right axillary region of burro No. 50, of the same group, on the 8th day. By the 10th day postshot it was observed that wounds were not healing. From that time onward until 28 or 30 days following the exposure, wounds had a rather fresh or static appearance, depending upon the degree of healing achieved prior to the second week. Consequently, incidental wounds were more noticeable especially over the leg joints, shoulders, and tuber coxae.

A summarization of the blood picture of several burros with obvious wound infective processes during the D + 8 to D + 12 period is given in Table 3.3.

Table 3.3—SOME BLOOD ELEMENTS IN BURROS WITH WOUNDS (D + 8 to D + 12)

Burro No.	Group	WBC	Granulocytes, %	Platelets X 10^3
64	IV	6,150	75	270
12	V	11,900	80	215
54	IX	4,100	70	195
72	IX	3,100	80	265
79	IX	5,500	87	310
92	IX	2,300	81	235
Control Av.		12,010	46	354

Following the initiation of a recovery process, subsequent to four weeks post detonation, a transitory rise in total leukocytes has been noted in separate animals with incidental wound infection. After several days the leukocyte counts dropped back to the preexisting low level consistent with the group level at that time.

Fig. 3.13—Infection of facial area Jennet No. 72, group IX, D + 5.

3.4.6 Epilation

Epilation was first observed on the 12th day postshot in a group VII animal, a large robust jennet which had given birth to a live foal 3 days previous. She survived an additional 9 days, during which she continued to shed hair to the extent of losing her entire mane. During the third week postshot epilation was seen in 16 additional animals; by D + 21, in 6 more; and by the 33d day, 27 showed alopecia. The extent of hair loss varied from almost complete alopecia to only marked shedding to the undercoat (Figs. 3.14 and 3.15). One striking aspect of the epilation was its occurrence on the back and one side of any affected animal. A correlation of the affected side with exposure position showed the hair loss to be confined to the side away from the blast. The distribution of epilation among survivors at 45 days by group is given in Table 3.4. Hair pulled easily from the bodies of other animals not classified as epilating; however, such observation is quite subjective.

Table 3.4—EPILATION BY GROUP (D + 45)

Group	No. affected
IV	1/1
V	1/1
VI	2/2
VII	3/3
VIII	3/6
IX	2/6
X	1/7
XI	2/8 (to undercoat)
All groups	15/34

3.4.7 Gonadal or Reproductive Effects

At no time following the detonation were exposed male burros observed to exhibit libido to the degree normally associated with the species. Prior to exposure the experimental jacks, and throughout the observation period the control jacks, exhibited normal expression of libido.

One female, No. 73, group V, was observed in estrus at D + 5. Rectal palpation revealed ovulation in the right ovary. At this time also a low-grade vaginitis was detected. She behaved as an animal in heat for 11 days and had a slight mucopurulent discharge from the vulva on

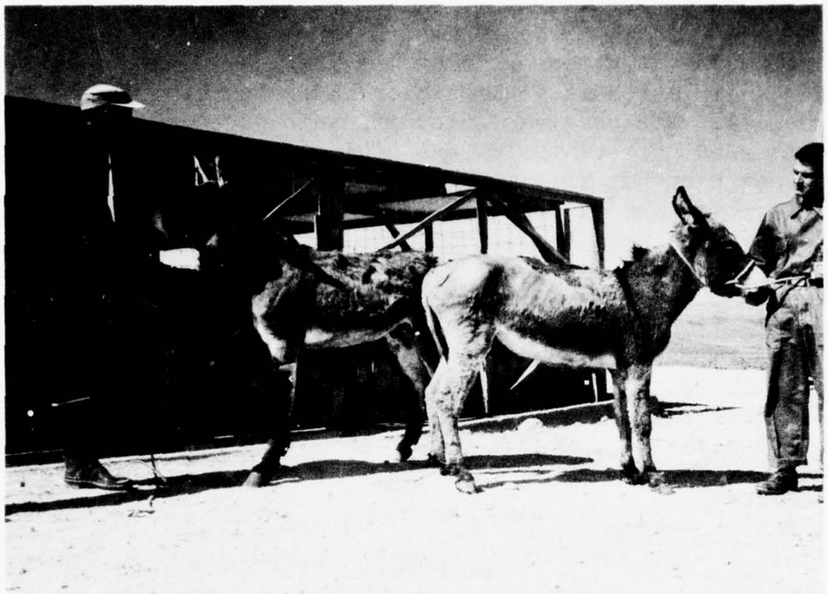


Fig. 3.14—Jack, group VII (right), showing almost complete alopecia over side and croup; group VIII animal (left) has spotty hair loss on left side.

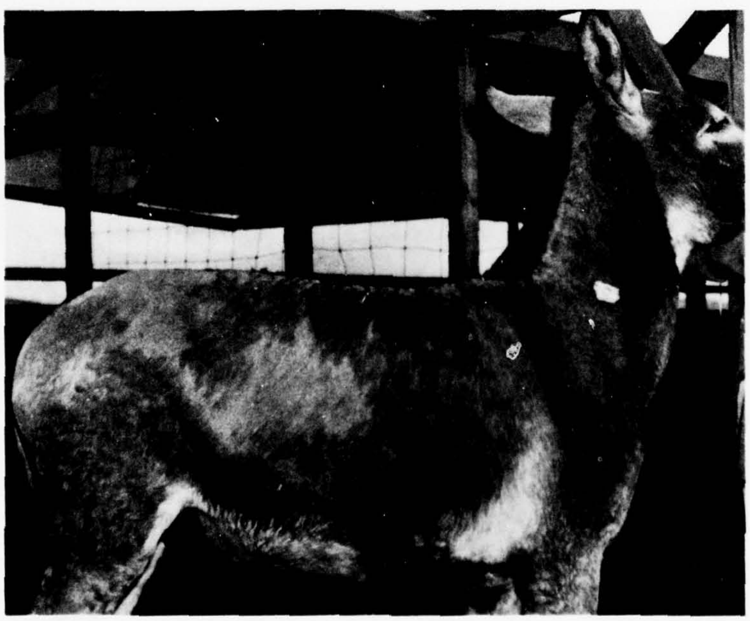


Fig. 3.15—Group X animal with marked shedding to undercoat.

the 11th and 12th. She died on the 24th day postshot, at which time the right ovary was found to contain a normal appearing corpus luteum. Both ovaries contained maturing follicles; however, no ova were observed in the sections available. The blood picture in burro No. 73 at the time of ovulation and within 4 days prior to death is given in Table 3.5.

Table 3.5—BLOOD ELEMENTS, BURRO NO. 73

Date	WBC	HT, %	Platelets X 10^3	Differential in % Seg.	Lym.	Immature
D + 5	3,000	43	375	27	44	16
D + 20	700	36	25	44	44	4
Preshot	10,500	44	455	71	26	0

Two exposed pregnant animals bore young during the period of observation. Burro No. 91, group VII, gave birth to a normal appearing but small (30 lb) male foal on D + 9. At the time of parturition the mother's white blood cell count was approximately 10 per cent of normal, with a platelet count of 160,000. The foal's early blood picture was within normal ranges; however, it weakened and died of starvation at 6 days of age. An apparently full-term normal appearing foal was born dead of burro No. 95, group X, on D + 29. The mother had shown no indication of imminent parturition. At this time her white cell count was 1300; hematocrit, 33 per cent; platelet count, 15,000. She showed no adverse effects from the experience and made a recovery consistent with the animals of her exposure group.

3.4.8 Clinical Classification of Nonsurvivors

(a) Animals Dying Within First Two Days. The high incidence of early mortality was associated with marked neurological symptoms. However, some animals collapsed or died quietly. The quiet deaths, those in which the prostrate animal appeared to be conscious and did not struggle, were all observed on the 2d day.

(b) Animals Dying Within First Week. During the balance of the first week, two animals exhibited severe neurological symptoms prior to death (3d day). One animal died quietly on the 3d day, and in an additional 6 animals death followed coma.

(c) Animals Dying Within Second Week. Burro No. 12, group V, was prostrate on D + 2. The following day it exhibited nystagmus and marked twitching and trembling. He arose on the 4th day to begin a subjective recovery which lasted until the 9th day. On D + 8 the animal was gaunt; there was an abscess draining below the left carpus; he showed a tendency to favor the left hind leg; and open sores were seen over the caps of both hocks. The animal continued to eat; however, on the 9th day appetite failed. A severe intermittent cough followed by throat clearing was noted along with grinding and snapping of the teeth. The animal was mean and recalcitrant at this time. Prior to death on the 10th day, the animal bled from the nose and showed the sign of forward pressing.

Animal No. 72, group IX, after recovering from neurological symptoms, died on the 12th day, following a massive infectious process over the facial area.

(d) Animals Dying After the Third Week. No deaths occurred in the experimental animal group during the third week. Burro 91, group VII, succumbed on the 22nd day following epilation and general loss of condition occurring over the 10 days previous. The animal was quiet and conscious prior to death.

Burro No. 73, group V, died on the 24th day after showing signs of inanition. The animal had previously recovered from neurological symptoms during the first week. She exhibited symptoms of foot pain on the 12th and 24th days. A mucopurulent discharge from the vulva and a yellow-tinged mucous discharge from the nostrils was seen 2 days prior to death.

Two animals of group VI died on the 25th day. Animal No. 88 died quietly after being down for 4 hr. On the day of death the animal was observed in a spraddle-legged posture pressing her forehead against the fence. During the course of her illness the animal had not previously shown signs of neurological involvement. Epilation begain on the 16th day, and a bleeding tendency was observed on D + 8. The other animal of group VI to die on the 25th day had recovered from early neurological symptoms, had epilated on D + 14, and had persistent nasal and eye discharge until death. Diarrhea was observed on D + 9 and on the day of death.

Burro No. 9, group V, recovered from early severe neurological symptoms and during the first two weeks had made a slow subjective recovery marked variously by eye discharge, epilation, and edema of the right front leg. The animal continued to improve until 3 days prior to death, at which time a rapid decline in general condition was observed with no singularly remarkable symptoms. This animal died on D + 30.

The death of burro No. 31, group VI, at 58 days was associated with capillary hemorrhage and dyspnea.. During the course of observation burro No. 31 had resumed eating at D + 4, shown diarrhea at D + 9, and epilation on D + 16. A wart infection was associated with a swollen, cracked,

bleeding muzzle. For two weeks prior to death this animal, in addition to the remarkable facial lesion, showed increasing alopecia, swollen and bleeding pressure sores on the leg joints, and apathy. His leukocyte count had gradually risen from 500 cells at D + 25 to 3000 cells prior to death. The platelet count had however remained at less than 50,000 since the second week postshot.

The last animal to die was No. 32, group VII. This animal had, in the days immediately postshot, been depressed and unable to stand. Subjective signs of recovery began on the 6th day with a gradual return of appetite. During the next four weeks the animal lost hair and remained in poor condition with moderate chronic discharge of the eyes accompanied by intermittent mucous nasal discharge. A severe wart infection involving the entire muzzle and eyelids of the animal lasted from the third to the eighth week. White blood cells and platelets reached minimum values (750 and <20,000, respectively) during the third week. White cells began to slowly increase at D + 30, and platelet counts rose steadily after the sixth week postshot. White cells returned to near the 3,000 level. The platelets dropped from 170,000 at the end of three months to none two weeks later, at which time the animal died.

3.5 HEMATOLOGY

3.5.1 General Response

The blood-element response to irradiation was graded in relation to dose position. The earliest notable observations were of an elevated leukocyte count on the 2d and 3d days postshot. Following this the WBC count decreased reaching minimal values during the fourth week. Hematocrit decline was slower to occur, followed by a platelet drop which also was maximum during the fourth week. Numerical recovery of white cells and platelets began following the fourth week and had reached nearly 50 per cent of normal values by the end of fourteen weeks. Recovery of the red cell system as measured by hematocrit values began after the sixth week with return to normal range by the end of fourteen weeks. Examination of hematological specimens has not yet been completed. For purposes of this report the 11 exposure groups were arbitrarily placed in three super groups representing high, medium, and low doses:

Group A, composed of groups I through IV
Group B, composed of groups V through VII
Group C, composed of groups VIII through XI

3.5.2 Leukocytes

Leukocytes in the peripheral blood showed an increase at 10 and 12 hr on shot day. One day later average WBC counts were approximately

twice the preirradiation values in the five highest dose groups (I - V) and in group VIII. The average WBC count of the lowest dose group (XI) was slightly below the preirradiation values. Figure 3.16 shows WBC changes in the three arbitrary groupings. During the observation period WBC counts in control animals averaged 11,730 ± 2,750.

A variety of atypical lymphocytes was noted in two groups (I and IV) examined 10 hr postshot. Morphological changes included fragmented nuclei, vacuolated cytoplasm, misshapen cell outlines, and eccentrically placed nuclei. A large proportion of the granulocytes was observed in immature form with O, U, and S shaped nuclei. Only scattered fragments of eosinophil cells were seen. Figure 3.17 represents efforts to picture the changed lymphocytes. Atypical cells were not observed in groups VII and X at H + 13 nor were they seen in group II at H + 24. Normal lymphocytes, for all practical purposes were nonexistent in all but the three lowest dose groups (IX, X, and XI) after the 2d day. Maximum depression of circulatory lymphocytes was observed between D + 2 and D + 3. Numerical recovery was apparent in all groups at D + 4. On the average, 45 days elapsed in all groups before a progressive positive increase was noticed. At the end of three months postshot, the average number of cells was 40 per cent of normal.

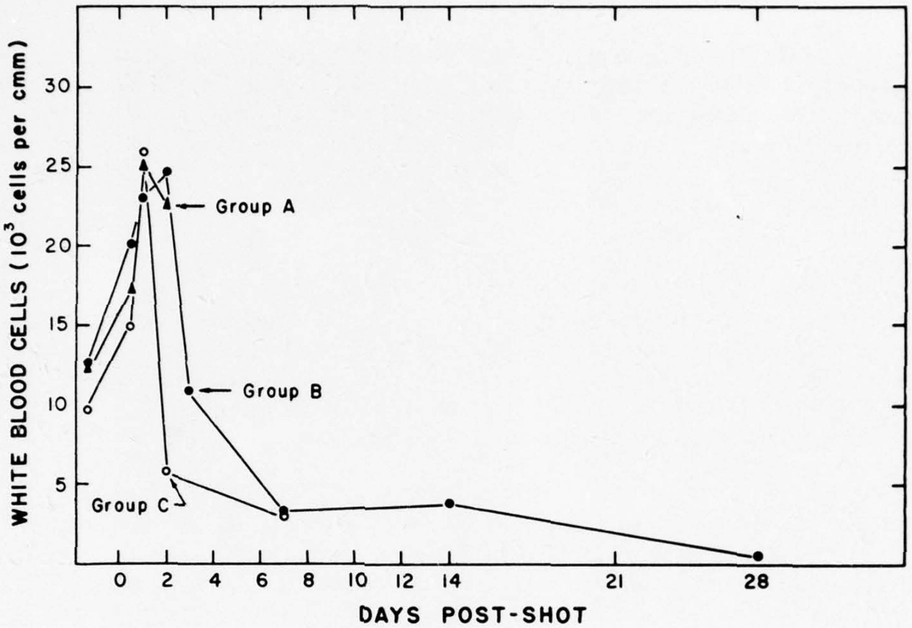
Segmented polymorphonuclear cells increased in all dose groups within the first 2 days postshot and accounted for the previously mentioned WBC increase. No decrease in segmented cells was observed in groups I, II, and III. In all other groups a decrease was apparent at D + 4, reaching minimal values between the third and fourth weeks. Numerical recovery followed, reaching the 50 per cent normal level at three months postshot.

Eosinophils disappeared from circulating blood immediately following exposure in all but the three lowest dose groups (IX, X, and XI). These cells had reappeared in surviving animals by the fourth day and persisted within normal ranges.

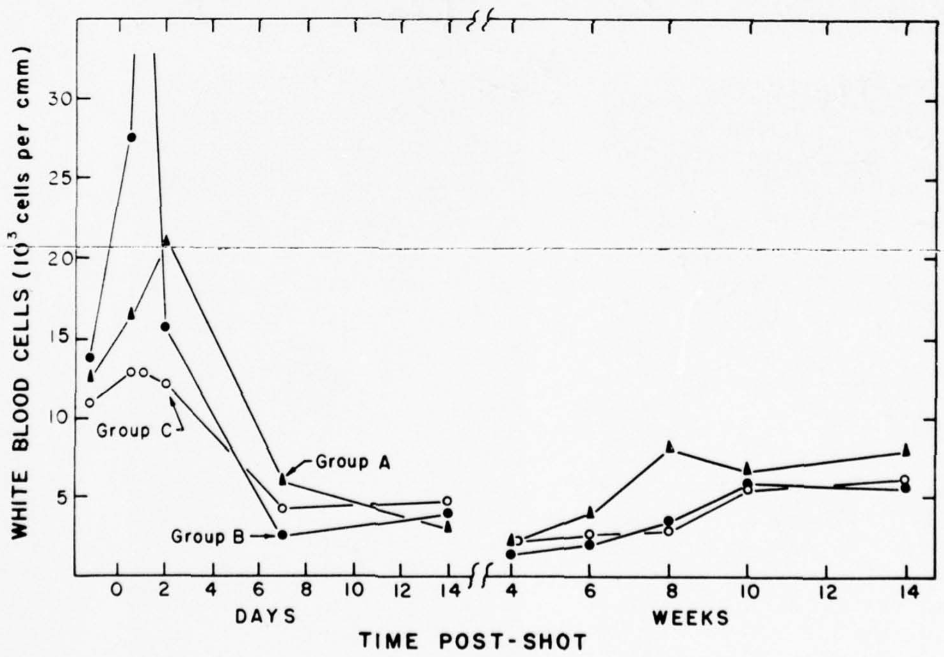
3.5.3 Platelets

A decrease in thrombocytes was notable in all groups between D + 5 and D + 10. Minimal levels were reached during the third week postshot. A positive increase in circulating platelets did not occur until D + 45. Within three months average counts in all groups had risen to 50 per cent of normal, or preirradiation, levels. During the period of platelet depression some of the animals survived over three weeks with counts of less than 20,000. Figure 3.18 shows the trend of averages in survivors and decedents.

After the first week following exposure, hematocrit values showed gradual decrease until the end of the fourth week. Recovery of hematocrit values began between the fourth and eighth weeks (Fig. 3.19).

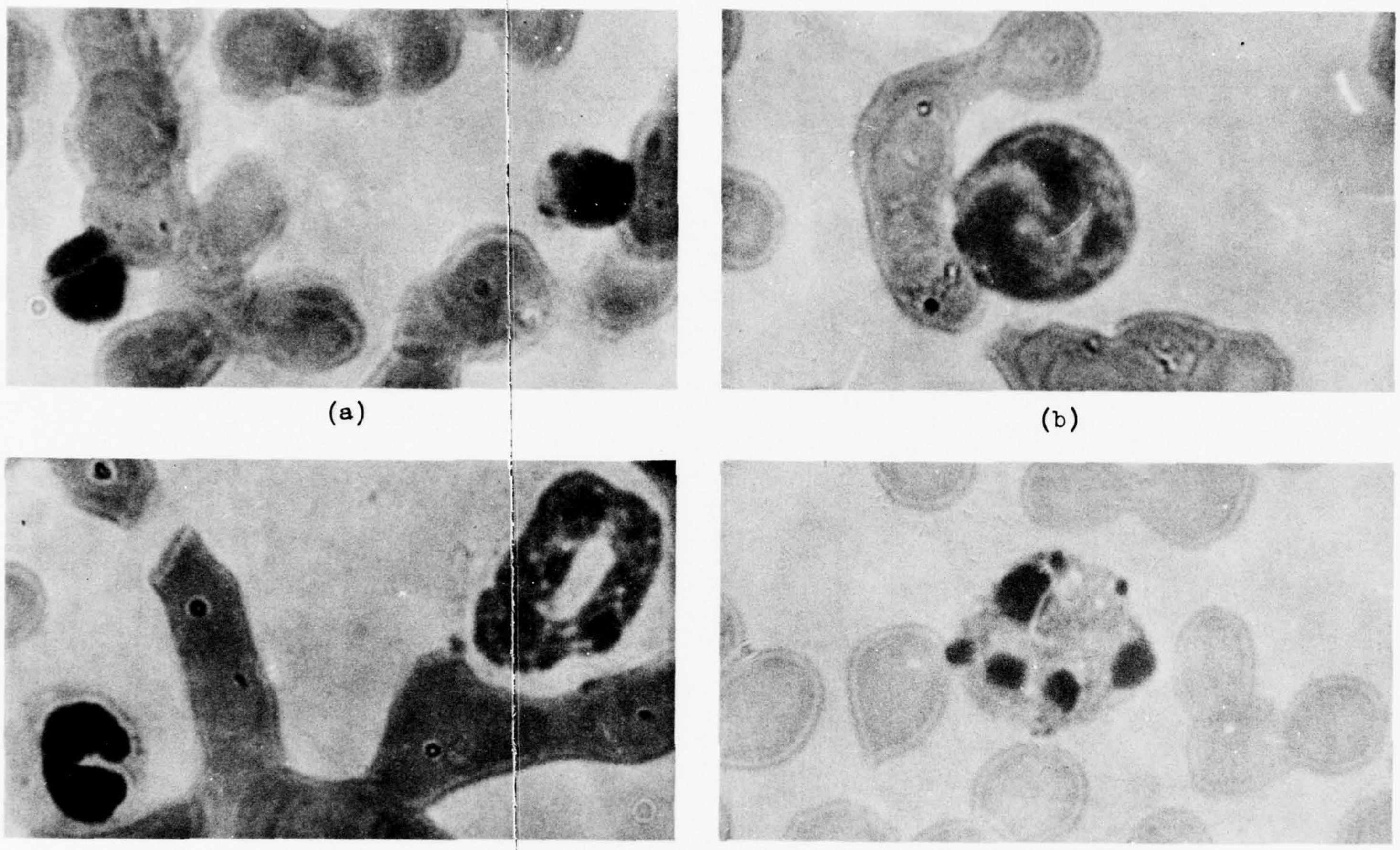


(a)



(b)

Fig. 3.16—(a) Trend of WBC average in nonsurvivors and (b) in survivors. Group A = groups I-IV; group B = groups V-VII; group C = groups VIII-XI.



(a) (b) (c) (d)

Fig. 3.17—Atypical lymphocytes from animals in groups I and IV at H + 10 showing: (a) bi-lobed lymphocytes and lymphocyte with nucleus off-center; (b) lysis of nucleus; (c) atypical lymphocyte and immature polymorphonuclear cell; (d) fragmentation of nucleus with vacuolization of cytoplasm.

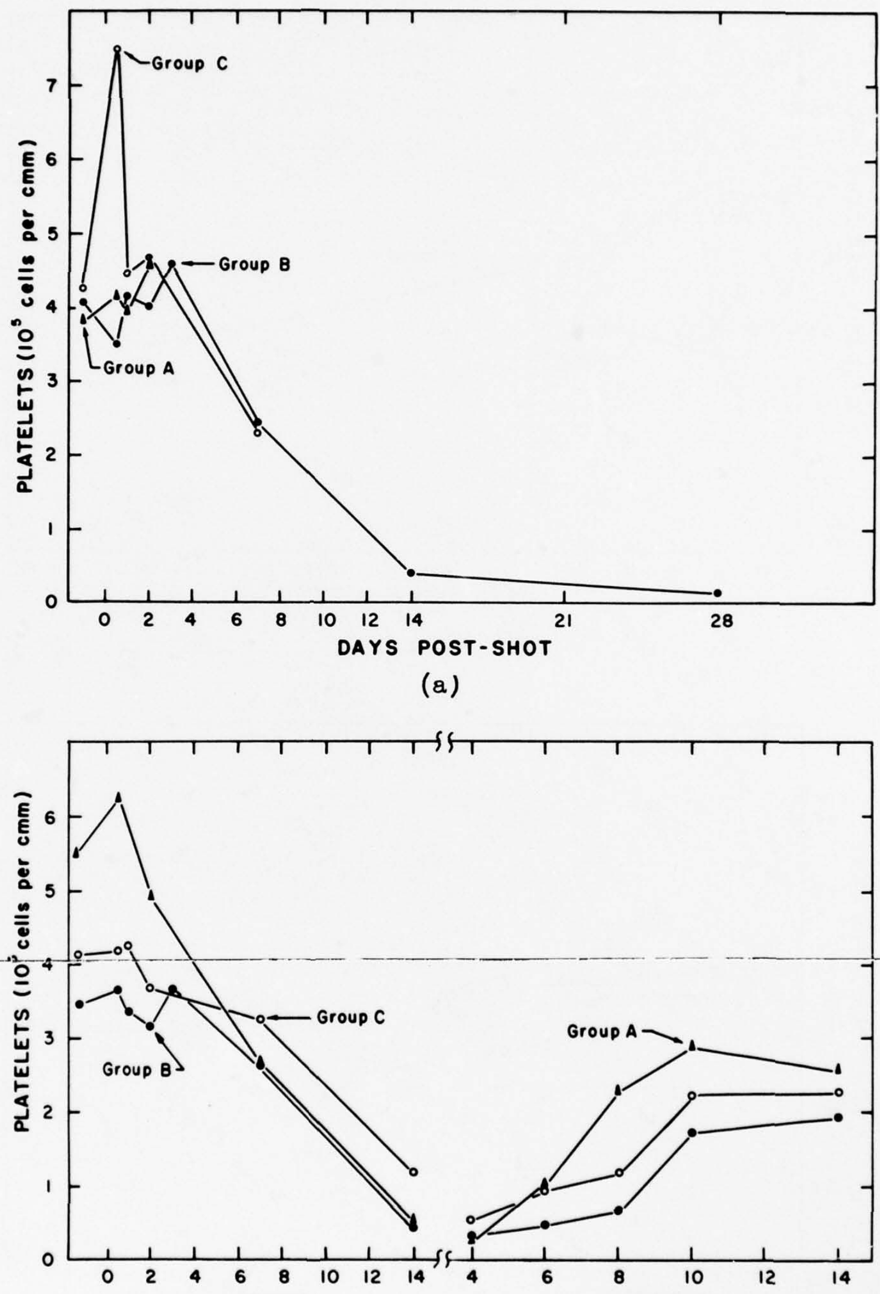


Fig. 3.18—(a) Trend of average platelet counts in nonsurvivors and (b) survivors. Group A = groups I-IV; group B = groups V-VII; group C = groups VIII-XI.

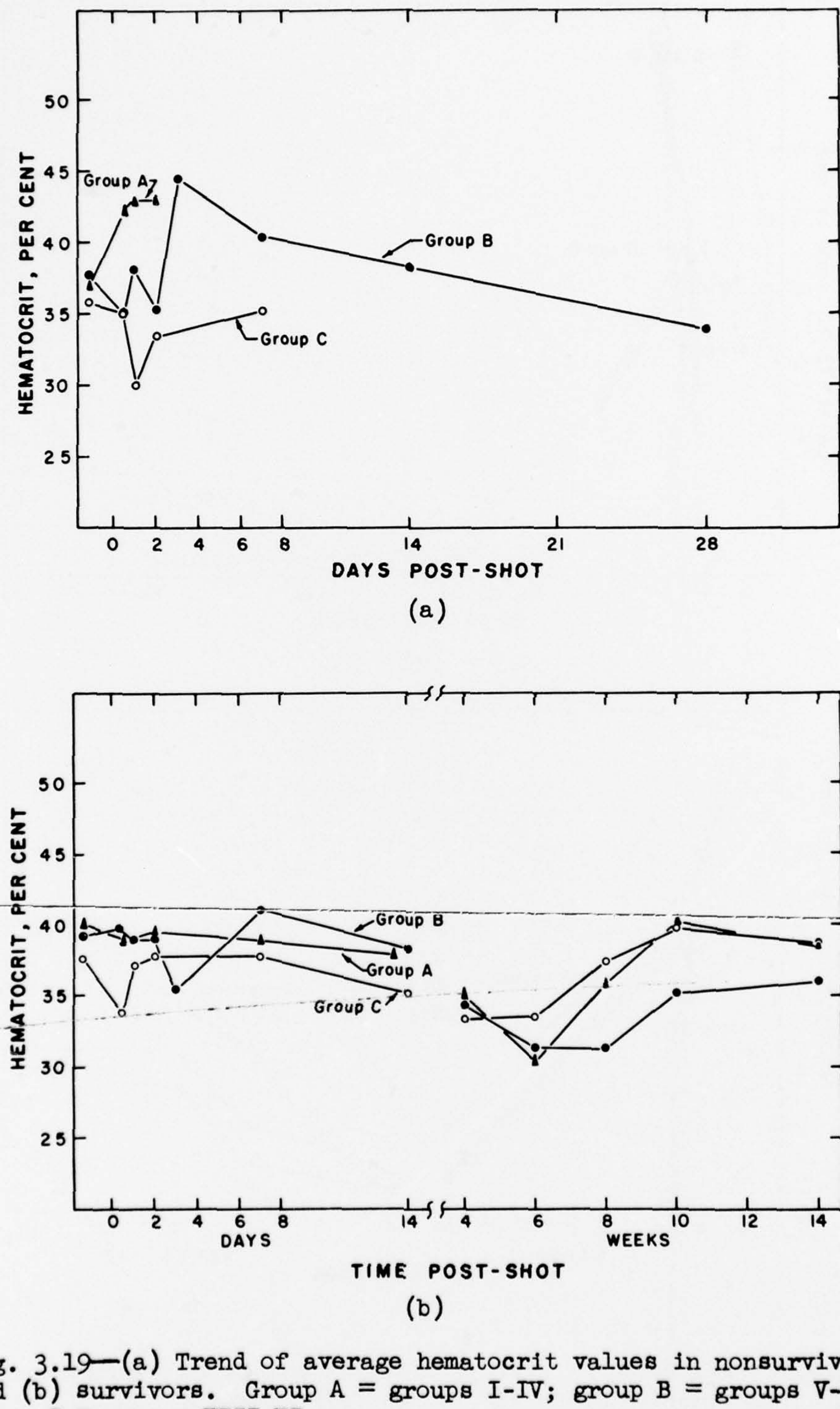


Fig. 3.19—(a) Trend of average hematocrit values in nonsurvivors and (b) survivors. Group A = groups I-IV; group B = groups V-VII; group C = groups VIII-XI.

A final report on this experiment will contain tabulations of all blood values by group.

3.6 WEIGHT CHANGES

The trend in body weights is shown in Fig. 3.20 for survivors and decedents. The changing population of the latter grouping limits of course the value of a line graph. However, from Table 3.6 an assessment may be made of the relative contribution of individual animals. Weight loss was real and significant in all groups. Surviving animals showed the start of weight recovery between one and two weeks postshot. Between the fourth and sixth weeks the average weight of groups VIII, X, and XI were equal to the preirradiation weights. By the end of the 17th week, only group XI had surpassed the preirradiation weight.

3.7 PATHOLOGY

Necropsy material collected at the Test Site has been partially reviewed. Information will be given in detail in the final report.

3.7.1 Animals Dying During the First Week

Evidence of gross pathological change in animals that died during the first 3 days was essentially negative. Some, but not all, of the animals exhibited wet, edematous lungs, congestion of the larger visceral blood vessels, and some hemorrhage of the serosal layers of internal organs. Subendocardial hemorrhage was variously seen in animals that showed evidence of agonal struggle. Petechial hemorrhage was visible in animals dying as early as H + 30 at the sites of parasite attachment. Exposure of the frontal and maxillary sinuses revealed nothing considered to be abnormal. Dissection of the middle and inner ear revealed nothing. Consistent changes noted in the histological examination of these early cases were perivascular cuffing in the brain and necrosis of lymphocytes. Perivascular cuffing with polymorphonuclear leukocytes was noted in the white matter of the cerebrum, cerebellum, and medulla. Destruction and necrosis of lymphocytes was observed in splenic follicles, lymph nodes, and lymphoid tissue of the gut.

Edema of the glottis and lungs was noted in one animal dying quietly on the 4th day. The following two deaths which took place on the 5th day showed hemorrhage of the adrenal cortices and some subpleural hemorrhage. Histological finding in these animals indicate a reduction in all lymphoid elements, congestion and small hemorrhage of the adrenals, and congestion and edema of the stomach and intestine.

Table 3.6—WEIGHTS OF DECEDENTS AND SURVIVORS*

Time	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
Survivors												
				(1)	(1)	(1)	(3)	(6)	(6)	(7)	(8)	(13)
D - 1 wk				370	380	426	380	378	362	348	355	362
D + 1 wk				327	342	393	317	344	320	328	328	373
D + 2 wk				348	336	406	323	359	334	339	350	
D + 3 wk				365	357	407	323	358	330	347	355	379
D + 4 wk				355	354	410	346	365	333	347	355	
D + 5 wk					362	413	338	369	342	349	365	390
D + 6 wk				356	354	421	359	377	355	358	370	
D + 7 wk				349	358	421	353	377	356	354	371	
D + 17 wk				340	346	402	337	370	349	337	370	382
Nonsurvivors												
D - 1 wk	350(8)	327(8)	349(8)	354(7)	333(7)	361(7)	327(5)	230(2)	270(2)	240(1)		
D + 1 wk					313(3)	305(4)	437(1)		250(2)			
D + 2 wk					310(2)	306(4)	372(1)					
D + 3 wk					308(2)	315(4)	348(1)					
D + 4 wk					250(1)	322(2)						
D + 5 wk						363(1)						
D + 6 wk						355(1)						
D + 7 wk						354(1)						

*Figures shown are mean weights in pounds. Figures in parentheses are number of animals.

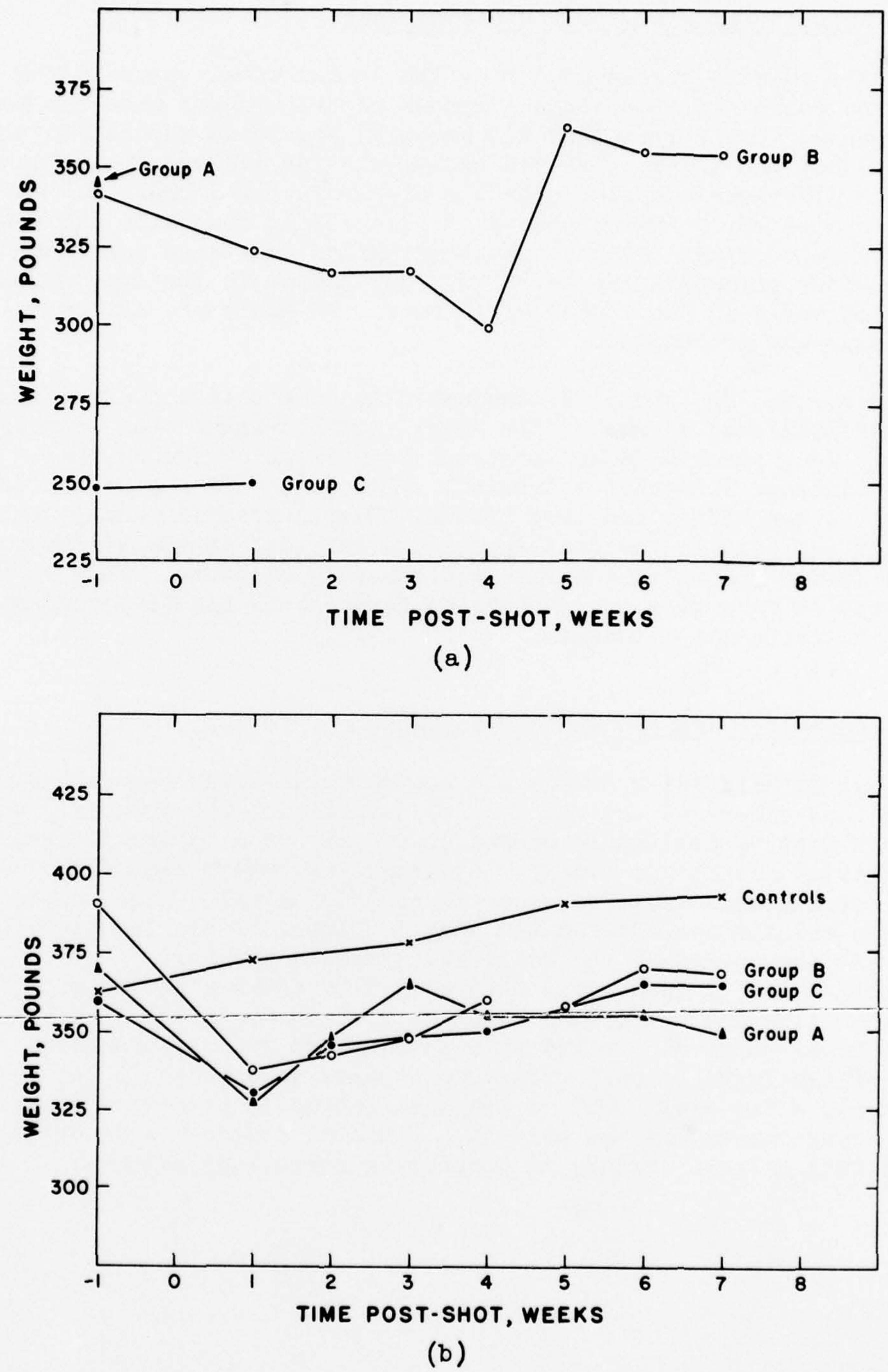


Fig. 3.20—Trend of body-weight averages (a) for nonsurvivors and (b) for survivors. Group A = groups I-IV; group B = groups V-VII; group C = groups VIII-XI.

3.7.2 Animals Dying During the Second Week

Three animals succumbed during the second week. Grossly the lungs contained edema and hemorrhage. Bronchial lymph nodes were swollen and hemorrhagic. One animal (No. 12, group V) had lungs suggestive of foreign-body pneumonia. Massive ecchymosis was present in the lung tissue with fibrinous adhesion over the diaphragmatic lobes. The animal had been down early in the course of illness and then made subjective signs of recovering. Microscopic examination confirmed the diagnosis of foreign-body pneumonia and revealed plant tissue in the lung probably aspirated early in the course of illness. In addition, atrophy of lymphoid tissue was pronounced.

Animal No. 72, group IX, succumbed 12 days postshot after sustaining self-inflicted wounds of the face. Gross changes seen on necropsy included lung hemorrhage and cortical hemorrhage of the adrenal. Microscopic findings indicated a terminal septicemia with bacterial foci present in the kidney and lung tissue. Vascularization and growth of connective tissue in the deep dermis and subcutis in the vicinity of the facial lesion indicated a marked inflammatory response. This was further demonstrated by a zone of lymphocytes beneath the tracheal mucosa. All lymphoid tissue was atrophic.

3.7.3 Animals Dying After the Third Week

Four animals dying during the fourth week showed hemorrhage of all viscera and ulcers of the mouth. One animal (No. 28, group VI) sustained a massive hemorrhage caused by rupture of a parasitic aneurysm of the anterior mesenteric artery. A dissecting hemorrhage of the longissimus dorsi muscle was also observed in this animal. Microscopic changes in these animals included septic emboli, hemosiderosis in the spleen, edema and congestion of the lung, and lymphoid atrophy.

Animal No. 31 (group VI) died at D + 58 after a period of progressive inanition and continuous bleeding from traumatized areas of the body. Gross changes revealed pale musculature and old organized hemorrhage of the lungs. Small focal hemorrhages were noted in the cerebral cortex and a few small foci of demyelinization in tracts of the pons. Acute bronchopneumonia was evident. Lymphoid tissue was somewhat depleted with a large variety in lymphocyte morphology evident.

Chapter 4

DISCUSSION AND CONCLUSIONS

The purpose of this report is not to attempt any far reaching generalizations from the response of the limited population involved. Presented here, to the best of our ability, is an objective report of the observations on the outcome of the experiment.

One of the striking features of the response was the pattern of early death, which was obviously dose related. Epilation has not been observed previously in burros following isotopic-source gamma irradiation. The median lethal response according to the measurements available was below those determined with radioisotopic total-body irradiation of burros.

Epilation occurred, for the most part, on the side of animals opposite the direction of the blast. We assume that scattered and degraded radiations were responsible for a skin dose sufficient to cause damage to the hair follicles. Previous total-body irradiation experiments with burros have not resulted in epilation. Nor have they been so oriented as to allow for an appreciable contribution to the total dose from relatively low-energy radiations.

It was interesting that prior to the second week the experimental animals were able to manifest an inflammatory reaction. Pus formation was remarkable until the circulating blood elements reached a level incapable of the natural reaction. Similarly, the estral cycle as observed in burro 73 was not interrupted prior to the formation of a corpus luteum at a time when platelet levels would support clot formation.

The early mortality response was dramatic and unexpected. However, two salient features of this response are to be noted. Death was associated with the period of acute neurological manifestations, and it was directly related to dose. As the dose decreased by group, a greater proportion of the animals were able to withstand the immediate insult and became either candidates for death associated with other mechanisms or survived. The survival times of decedents after the first 4 days were

within ranges previously experienced with radioisotopic irradiation, and the pathological changes followed a similar pattern. The early death response was the more dramatic because of the numbers involved, 100 per cent mortality being experienced by the first three groups within 3 days. Possible contributary factors include the effects of neutrons, not previously applied to burros, and the instantaneous dose rate. Reviewing the mortality pattern following radioisotopic total-body exposure,[1-4] it is observed that following exposure to Co^{60} burros exhibited a bimodal death pattern with peaks at 3.2 and 26.5 days. All animals dying within 5 days following removal from the exposure field exhibited encephalitis-like symptoms. The maximum dose rate was 50 r/hr. Burros exposed to Ta^{182} at the rate of 20 r/hr showed a unimodal death pattern beginning at the 20th day postexposure. In the depth-dose study described in this experiment, the thermal neutrons detected in the head were approximately twice those detected in the body of the animal. This is unexplained.

To throw light on the possible effect of at least one variable, i.e., dose rate, two animals were exposed under laboratory conditions to Co^{60} irradiation of the head only. The rate was 3400 r/hr. One animal received 1480 r, which is analogous to the dose received by group I on the basis of comparison of the $LD_{50/30}$ for the experiment and that established for Co^{60} (402 vs. 784). This animal exhibited profound depression followed by symptoms of encephalitis; it survived 14 hr. Another animal was similarly given 785 r and, after exhibiting neurological symptoms, succumbed at 29 hr and 45 min. These studies are being continued at the present time. If possible, an LD_{50} for Co^{60} at high dose rates will be established in the burro.

The median lethal dose of 402 ± 2 rep from the detonation is considerably lower than those established with radioisotopic radiation:

$LD_{50/30-45}$ days	Source
784	Co^{60}
651	Ta^{182}
532	$Zr\text{-}Nb^{95}$

The gamma-ray depth dose from the detonation was similar (70 per cent of air dose) to those measured for isotopic sources. The median lethal dose then implies a possible greater effectiveness for the neutron component of the prompt radiation. The implication would assume no influence from dose rate. Such comparison must take into consideration the fallibilities inherent in the median lethal dose as a measure of effect. For instance, the animals comprising the experimental population for this study were divided into two groups on the basis of weight, i.e., the four heaviest and four lightest of each exposure group. When they were treated as separate populations, the derived LD_{50} for each group (Fig. 4.1) was found to be:

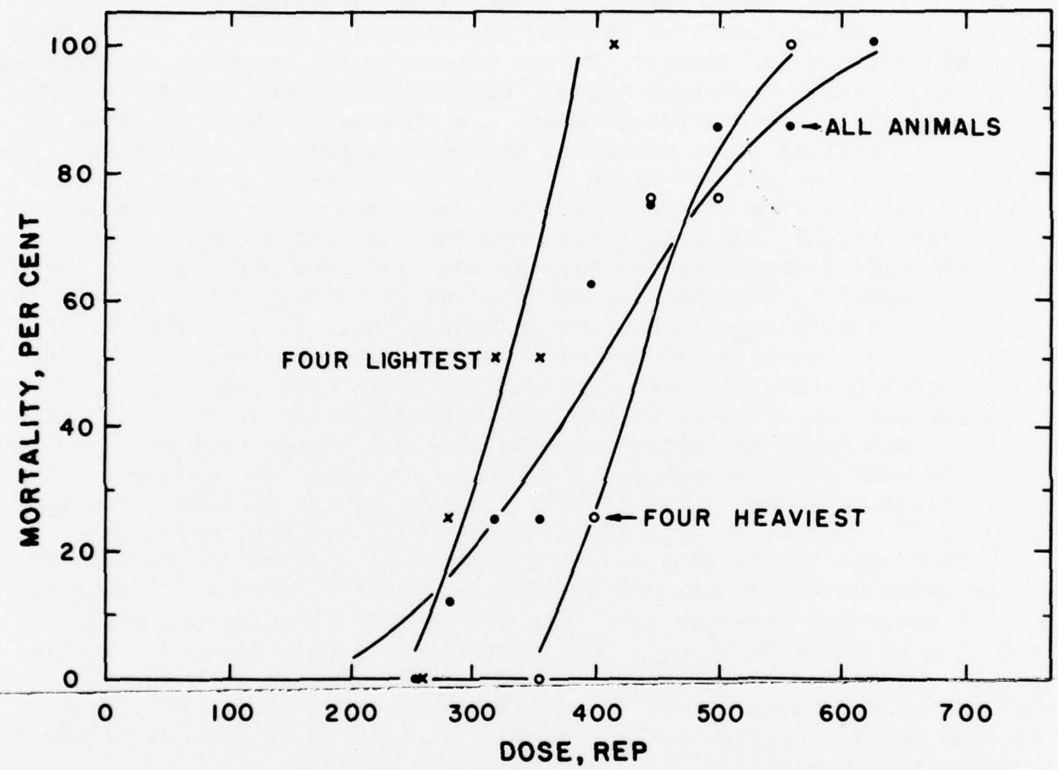


Fig. 4.1—Cumulative mortality by weight groups.

		$LD_{50/30}$
4 heaviest animals (groups IV through VIII)		434.9 ± 2.5 rep
4 lightest animals (groups VII through XI)		316.6 ± 19.3 rep

There exists a natural inclination among interested persons to make extrapolations from radiation effects in the burro to man. And indeed this is the basic reason for the animal experimentation. There are many marked similarities between the radiation syndrome in the burro and that reported for humans: Burros cannot vomit; however, anorexia and drooling are early transient signs. Following a latent period the characteristics of the radiation sickness are similar to those reported in humans. A critical point is passed at approximately 30 to 40 days. Recovery time for weight and blood elements is inversely proportional to dose and extends over a 2-year period. These and other similarities, i.e., size, weight, and weight distribution, do invite comparisons. There are also dissimilarities between the burro and man. One of these is not necessarily the high incidence of early mortality experienced in these first burros exposed to fission radiations. It is not known whether or not humans would suffer a high incidence of early mortality if subjected to identical exposure conditions as were these animals. For these and many reasons we feel that extrapolation of radiation effects in burros and other experimental animals to man should best be kept within the purview of individuals qualified to interpret and estimate radiation effects in humans. The data in this report are intended to augment the body of information upon which to possibly base such estimates.

Within the limitations of the experimental design, the objectives of the study have been reasonably attained as of this date. Normalization of the burro response with that of the monkey awaits the complete reporting of the experimental data pertaining to both species. Interesting comparisons have been made between the response of burros to prompt fission radiation and to radioisotopic irradiations up through the time period covered by this report. It will be of great interest to continue this comparison in regard to latent damage.

As with any experimental study, questions ancillary to the original were soon raised. It would be interesting to know the actual effectiveness of neutrons in the burro in relation to dose, dose rate, and energy, and these in regard to various biological end points. Also, it would be interesting to know the exact influence of these relations for gamma radiation. An extension of the preliminary high gamma dose rate studies mentioned previously seems to offer one means of separating rate and effect of type of radiation. This we feel should be continued. The question remains: "What is the dose in terms of expended energy to organs and organ systems?" From the standpoint of protective measures and the ultimate possibility of therapeutic intervention, if the burro is to be used as one species upon which to base extrapolation of effects to man, it will be necessary to know where and when these radiations are effective.

It is our sincere opinion that our most worth-while efforts could be directed to further dosimetric studies utilizing chemical systems in burro phantoms which could be compartmentalized into organ systems. The anticipated development of small neutron detectors and chemical dosimeter assemblies offers exciting possibilities for dosimetry studies in large animals during future weapons test participation. These could be utilized in cadaver depth-dose studies in conjunction with chemical-system phantom studies to furnish the needed correlation with effect.

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APPENDIX A

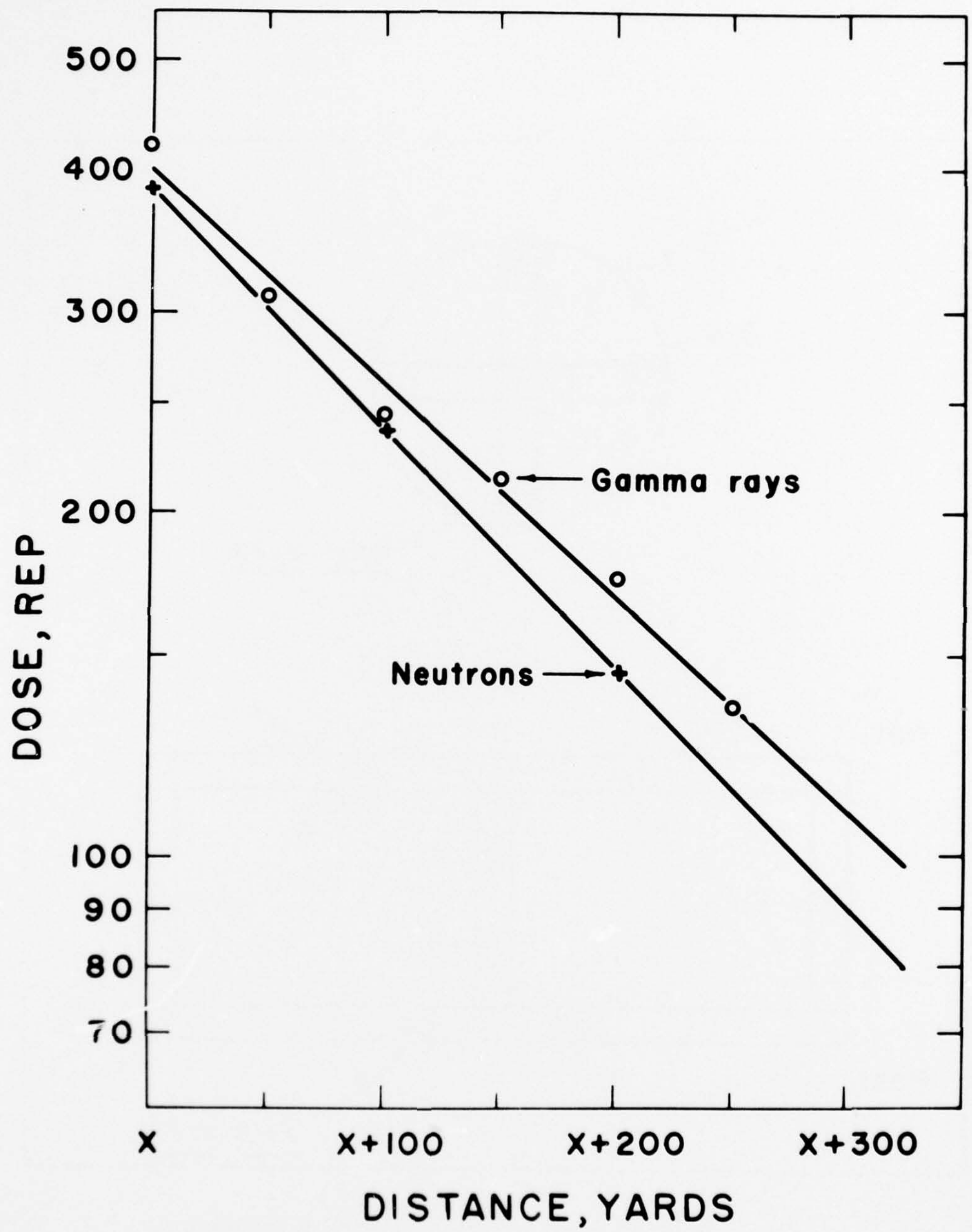

Fig. A.1—Least-squares treatment of dosimeter measurements for interpolated values.

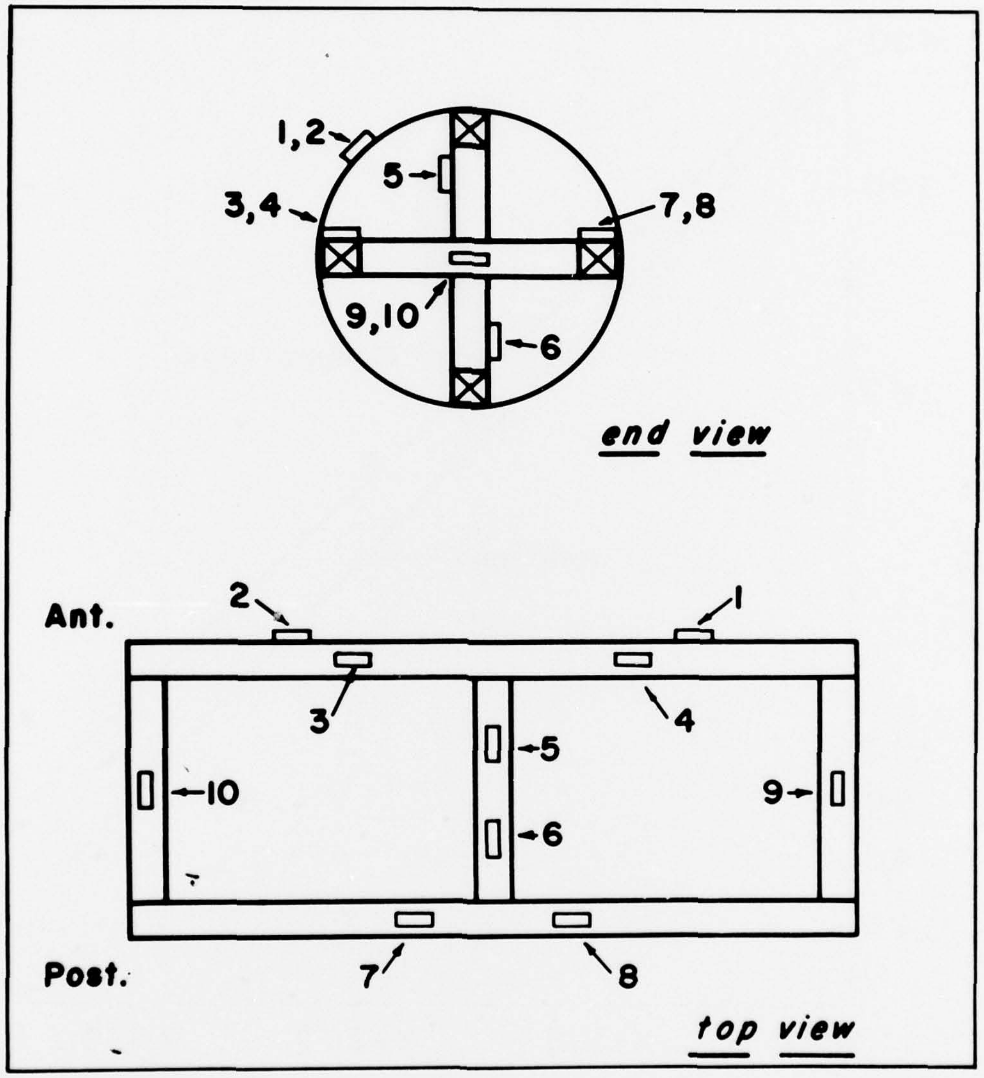

Fig. A.2—Film-badge positioning within shelters.

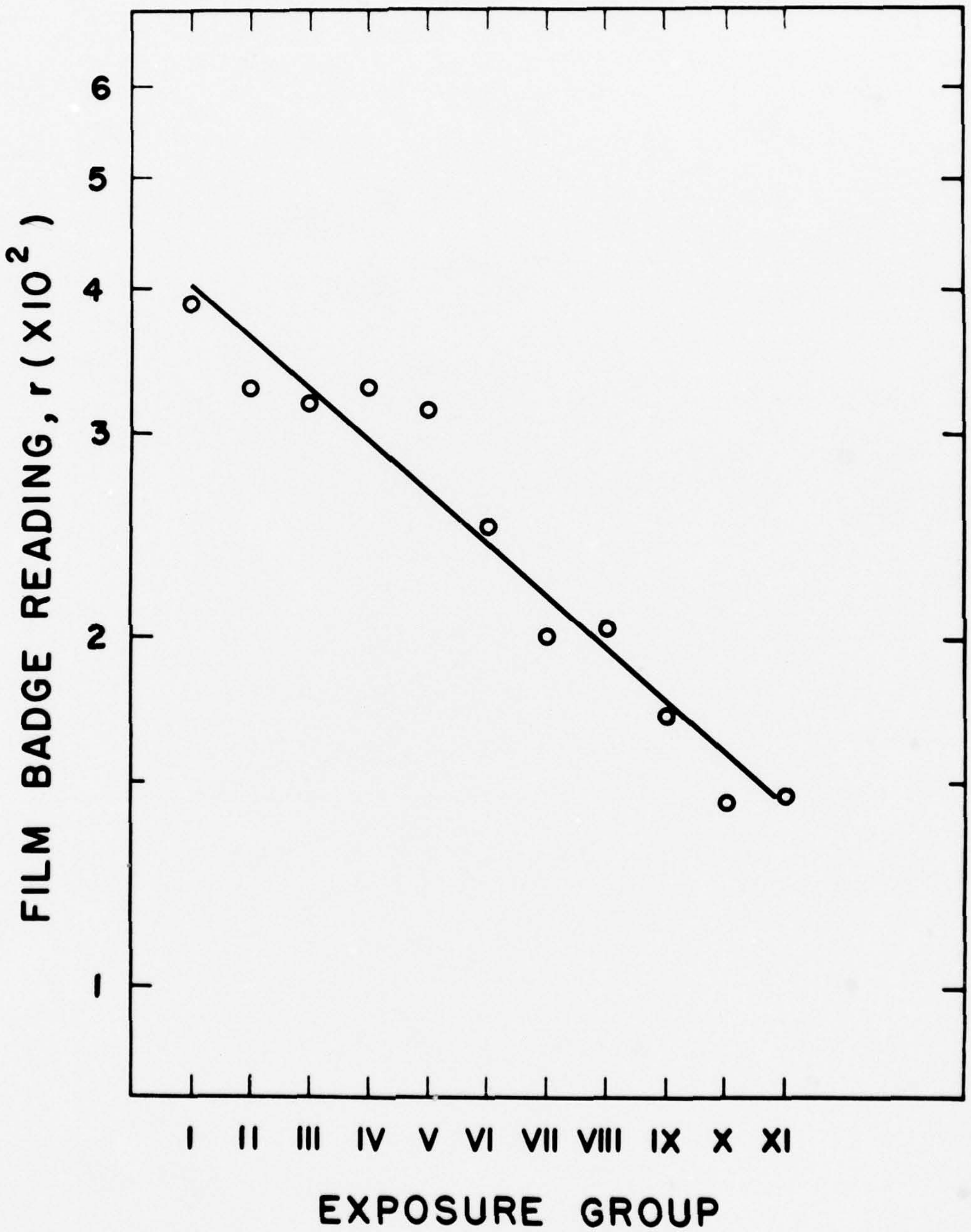

Fig. A.3—Film-badge readings in relation to station and position.